

# **CUTANEOUS HYPOPIGMENTATION: A STUDY OF 300 CASES**

Dissertation Submitted in  
fulfillment of the university regulations for

**MD DEGREE IN  
DERMATOLOGY, VENEREOLOGY AND LEPROSY  
(BRANCH XII A)**



**THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY  
CHENNAI**

**MARCH 2008**

# **CERTIFICATE**

Certified that this dissertation entitled “***CUTANEOUS HYPOPIGMENTATION: A STUDY OF 300 CASES***” is a bonafide work done by **DR ANKIT AGARWAL**, Post Graduate Student of the Department of Dermatology and Leprosy and Institute of Venereology, Madras Medical College, Chennai – 600 003, during the academic year 2005 – 2008. This work has not previously formed the basis for the award of any degree.

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## **SPECIAL ACKNOWLEDGEMENT**

My sincere thanks to **Prof. T. P. Kalaniti**, M.D., Dean, Madras Medical College for allowing me to do this dissertation and utilize the institutional facilities.

## ACKNOWLEDGEMENT

I am gratefully indebted to **Prof.Dr.B.PARVEEN, MD.DD**, Professor and Head, Department of Dermatology and Leprology for her invaluable guidance, motivation and help throughout the study. I would like to express my sincere and heartfelt gratitude to **Professor Dr.V.S.DORAIRAJ, M.D., D.V.**, Director, Institute of Venereology.

I wish to thank **Dr.N.Gomathy M.D., D.D.**, Former Professor, Department of Dermatology and **Dr.N.Usman M.D., D.V., PhD**, Former Director, Institute of Venereology for their constant support and motivation.

I am grateful to **Dr.S.Jayakumar M.D., D.D.**, Additional Professor, Department of Dermatology for his invaluable guidance and help. I sincerely thank **Dr.C.Janaki M.D., D.D.**, Additional Professor, Department of Dermatology (Mycology) for her priceless support. I thank **Dr.N.Kumar M.D.D.V.,D.M.R.D.** Additional Professor, Institute of Venereology for his guidelines.

I express my earnest gratitude to **Dr.D.Prabhavathy MD.DD**, Professor and Head, Department of Occupational Dermatology and Contact Dermatitis for her constant motivation and guidance. I thank **Dr.V.Somasundaram MD.DD**, Additional Professor, Department of

Occupational Dermatology and Contact Dermatitis for his benevolent help and support.

My sincere thanks go to Dr.G.K.Tharini, M.D., Dr.V.Anandan M.D.,D.C.H.,D.N.B.(Paediatrics) Dr. R. Priyavathani, M.D., D.D., D.N.B., Dr. N.Hema, M.D. and Dr.S.Anupama Roshan D.D.V.L , Assistant professors Department of Dermatology for their kind support and encouragement.

I thank Dr. A. Hameedullah, M.D., D.D., Dr.S. Kumaravelu, M.D., D.D., Dr. J. Manjula, M.D., DNB and Dr. Afthab Jameela Wahab M.D., D.D., Assistant Professors for their support and help.

I am inclined to thank Dr.V.Thirunavukarasu M.D.,D.V., Dr.K.Venkateswaran M.D.,D.V., Dr.S.Thilagavathy M.D.,D.V. Dr.P.Mohan M.D.D.V., Dr.S.Arunkumar M.D.D.V., Dr.S.Kalaivani M.D.D.V and Dr.P.Prabakar, M.D. (DVL), Assistant Professors, Institute of Venereology, for their help and suggestions.

I express my sincere gratitude to **Dr.P.Rathinavelu MD., DD.,** Former Professor of Leprosy and Dr.R.Arunadevi MD., DD., Lecturer/Registrar, Department of Dermatology for their support.

I duly acknowledge the paramedical staff and my colleagues for their help and favors. Last but not the least I am profoundly grateful to all patients for their co-operation and participation in this study.

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## **Introduction**

Skin is the largest organ of the body and the only organ which is visible and is in direct contact with the environment

It has been said that the greatest problems in this world are very tiny, the atom, the ovum and a touch of pigment. The largest organ of the body very commonly suffers from this touch of pigment.

Numerous skin conditions cause alteration in the normal pigmentation resulting in significant psychological morbidity due to cosmetic disfigurement.

Pigmentary disturbances may be congenital or acquired, circumscribed or generalised, hypomelanotic or hypermelanotic. This study strives to study the various skin conditions presenting as hypopigmentation. With attention to variability of extent of hypomelanosis, history of evolution, attention to hue and awareness of ancillary features, the differential diagnosis will be narrowed down and definite diagnosis will be arrived at with the help of relevant investigations. An attempt will also be made to find the relative incidence of each condition.

## **Review of literature**

### **Colour of the skin**

Normal colour of the skin is dependent on <sup>1</sup>

1. Hemoglobin (both oxygenated and reduced state)
2. Carotenoids
3. Melanin pigment

The major colour determinant is melanin and the racial and ethnic differences in skin colour are related to the number, size, shape, distribution and degradation of melanin-laden organelles called melanosomes which are transferred to the surrounding epidermal keratinocytes.<sup>2</sup>

Two types of melanin pigmentation occur in humans <sup>3</sup>

1. Constitutive skin colour : amount of melanin pigmentation that is genetically determined in the absence of sun exposure and other influences
2. Facultative (inducible) skin colour or tan : results from sun exposure



## **The Melanocyte**

The melanocyte is a dendritic, pigment synthesizing cell derived from the neural crest that is confined mainly to the basal layer.

Events that govern melanocyte distribution and function include <sup>4</sup>

1. Migration of melanoblasts from the neural crest, proliferation and localization in the skin and other tissues
2. Activation of specific cell surface receptors that transmit environmental signals for survival, proliferation and pigmentation
3. The expression of key enzymes and structural proteins responsible for melanin synthesis
4. Maintenance of proper ionic environment within secretory system conducive to maturation and activity of key enzymes and to melanosomal organization
5. Transport of melanosomes to dendrites and their transfer to epidermal keratinocytes

## **Embryology<sup>5-8</sup>**

From the precursors in the neural crest, melanocytes migrate to the epidermis, various epithelia of the mucous membranes, hair follicles, dermis, leptomeninges, inner ear, choroid, part of iris, peripheral nerves, the sympathetic chain and the lining of the coelomic cavity

Primitive melanocytes in the skin are first found in the eighth week of fetal life. These cells do not produce melanin actively until after intrauterine life ends and postnatal life begins except in certain sites like nipples and genitalia. By the 10<sup>th</sup> week these cells contain melanosomes. Melanocytes in skin continue to reproduce themselves by cell division although mitotic melanocytes are rarely seen in vivo

## **Development**

### **The Early signals<sup>9-11</sup>**

Induction of formation of neural crest is as a result of

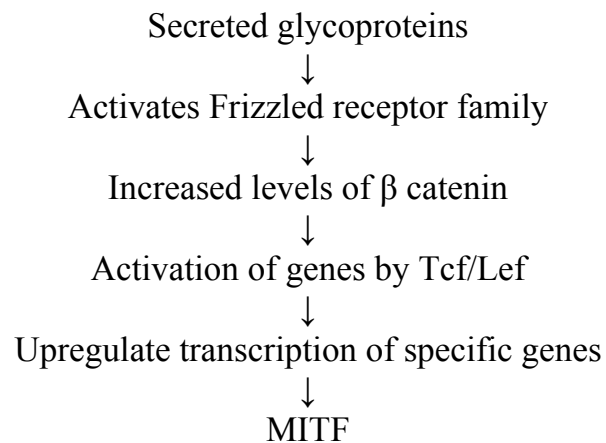
1. Members of Wnt
2. Fibroblast growth factor

3. Bone morphogenetic protein families
4. Noelin-1

Positive signals for melanocyte development emanate from

1. Wnt/ $\beta$  catenin
2. The receptor tyrosine kinases kit & met
3. G protein linked multiple membrane spanning receptor endothelin B
4. The cell surface adhesion molecules cadherin

Wnt /  $\beta$  Catenin



MITF (Microphthalmia transcription factor) <sup>12</sup>

Promotes transition of precursor cells to melanoblasts

Role in melanoblast survival by influencing kit expression

### **Receptor tyrosine kinases**

STEEL/ C-KIT (Mast/ Stem cell factor)

Essential for the development of early melanocyte precursors

Heterozygous loss leads to failure of melanocytes to populate broad cutaneous zones

Homozygous loss leads to complete absence of melanocytes

Presence of STEEL factor in keratinocytes contributes to melanocyte localization in the epidermis

HGF/MET (Hepatocyte Growth Factor or Scatter Factor) <sup>13</sup>

Activation of MET by its ligand, HGF is required for melanocyte viability and proliferation during development

Other factors involved

Endothelins & Endothelin receptor B<sup>14</sup>: growth factors whose mutations produce neural crest defects

Cadherins (calcium dependent surface receptors)<sup>15</sup>: mediate cell adhesion, homing and invasion

SOX10 & Pax3<sup>16</sup>

### **Epidermal melanin unit<sup>17</sup>**

Each epidermal melanocyte is surrounded by a group of keratinocytes with which it maintains functional contact, the whole being an epidermal melanin unit. A single melanocyte supplies melanosomes to a group of 36 keratinocytes.

### **Distribution<sup>18</sup>**

Total melanocyte population is about  $2 \times 10^9$  cells. The density of melanocytes ranges from  $2900 \pm 249/\text{sq mm}$  for the face to  $1100 \pm 215/\text{sq mm}$  for the upper arm or trunk. There are no sexual or racial differences

**Structure**<sup>19,20</sup>

When viewed through conventional microscope melanocytes appear as clear cells in and immediately beneath the basal row of the epidermis which is an artifact due to shrinkage of cells. Cytoplasm is dendritic and the dendrites arborize in all directions. Nucleus is smaller and more deeply basophilic than basal keratinocyte.

On hematoxylin eosin staining average number of melanocytes is one out of 10 cells in the basal row

On electron microscopy a melanocyte is seen to contain numerous mitochondria, well developed rough endoplasmic reticulum, prominent golgi apparatus and cytoplasmic filaments. They lack desmosomes and tonofilaments<sup>20,21</sup>

**Melanosomes**

Characteristic feature of melanocytes is the presence of special cytoplasmic organelles called melanosomes which are membrane bound granules of size 200 X 900 nm and in which melanin synthesis takes place.<sup>22</sup>

Secretory melanocytes produce melanosomes that are transferred to surrounding keratinocytes<sup>23</sup>

Non secretory melanocytes called melanophores do not transfer the melanosomes but redistribute them within the cell

Four stages of melanosomal development are identified<sup>24</sup>

1. Stage 1: Spherical, membrane bound vesicles longitudinally oriented concentric lamellae
2. Stage 2: Oval. Numerous lamellae. Melanin deposition begins at this stage.
3. Stage 3: Electron dense melanin, partially obscuring the network of internal lamellae
4. Stage 4: Fully developed & electron opaque. Dense deposits of melanin with vesiculoglobular bodies

During progression from stage 1 to 4 tyrosinase decreases and acid phosphatase increases.

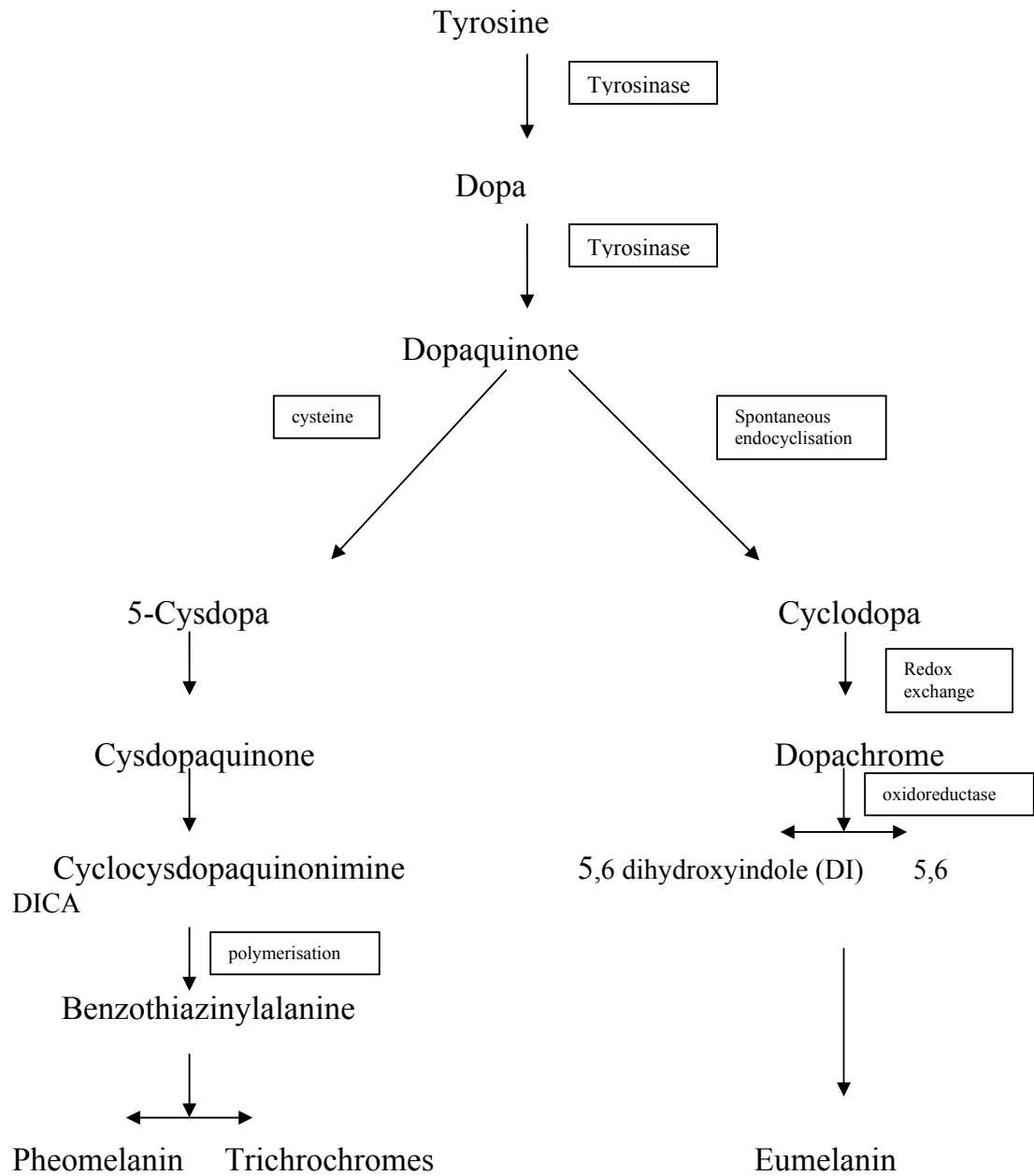
## **Melanin and melanogenesis**

Melanin is a heteropolymer. In humans three major classes of integumentary melanin are seen<sup>25,26</sup>

1. Eumelanin : manufactured by ellipsoidal melanosomes and responsible for brown and black colour of both skin and hair
2. Pheomelanins: produce in spherical melanosomes and accountable for the lighter colours of hair from yellow to reddish brown
3. Trichochromes: sulphur containing pheomelanin pigments with well defined structure characterised by a chromophore



# Melanin synthesis pathway<sup>25</sup>



Vesiculoglobular bodies are thought to be involved in the internal organization and melanisation of both eumelanosomes and pheomelanosomes.<sup>27</sup>

Intracellular transport of melanosomes from their formative zone in the perinuclear Golgi region to the tips of the melanocytic dendrites is considered to be mediated by cytoplasmic filaments.<sup>28</sup>

### Apocoptation<sup>29</sup>

Once melanosomes are formed, melanised and transported to the tips of dendrites, they are transferred from the melanocytes to keratinocytes by apocoptation i.e. a process of snipping off the tips of dendrites by keratinocytes. In the process keratinocytes phagocytize the melanosome laden tips of melanocytic dendrites. This results in collections of melanosomes being situated within both epidermal and follicular keratinocytes.

In the epidermis melanosomes become concentrated in an umbrella like array above the nuclei of keratinocytes.

Following transfer to keratinocytes, melanised melanosomes are conveyed upward as basal keratinocytes mature and eventually are

degraded by lysosomal enzymes and shed as cornified cells are desquamated

#### Endocrine and paracrine influences

Hormones such as melanocyte stimulating hormone (MSH), adrenocorticotrophic hormone (ACTH), lipotropins, estrogens, progesterone, thyroxine and androgens all possess melanocyte stimulating capability.<sup>30,31</sup>

Other physiologic stimuli include prostaglandins  $E_2$  and  $D_2$ , arachidonic acid, oleic acid<sup>20</sup>, leukotrienes  $C_4$  and  $D_4$ <sup>32</sup>, basic fibroblast growth factor<sup>33</sup>

#### Effect of ageing and UV radiation<sup>34</sup>

On exposure to UV radiation melanocytes increase in number and size and become more dendritic. Furthermore the process of synthesis of melanosomes, melanisation of melanosomes, transport of melanosomes to dendrites and transfer of melanosomes to keratinocytes are all accelerated. Melanosomes become larger and more heavily melanised.

Ageing is accompanied by a decline in number and activity of follicular melanocytes. Epidermal melanocytes also decline in number with ageing

Biological significance of melanin <sup>2, 35-37</sup>

Various functions attributed to melanin are

1. Protection of lower layers of skin against UV light by diffusing and absorbing the light
2. Elimination of genetically damaged cells by a phototoxic mechanism
3. Acts as a stable free radical and thus may act as a trap for electrons and free radicals
4. Can participate in oxidation reduction reactions
5. Melanin circulating through the body may influence intracellular metabolism and thus can be regarded as a hormone

## **Disorders of melanin pigmentation**

There are three categories of melanin pigmentary disturbances<sup>38</sup>

1. Hypomelanoses : lack of pigment in skin
2. Brown hypermelanosis (melanoderma) : epidermal hyperpigmentation
3. Gray, slate or blue hypermelanosis (ceruloderma) : dermal hyperpigmentation

### **Hypomelanoses<sup>2</sup>**

Hypomelanosis: lack of pigment in the skin which therefore appears white or lighter than the normal colour

Amelanosis: total absence of melanin in the skin

Depigmentation: loss of preexisting melanin pigmentation

Leukoderma: It is defined as a white skin or skin lighter than the normal skin of a person that may be congenital or acquired and can be due to variety of etiological factors

## **Clinicopathological classification of hypopigmented lesions <sup>39</sup>**

Melanocytopenic: due to absence or loss of melanocytes

Melanopenic: due to failure of normal melanocyte function

Non melanotic : not melanin related

### Melanocytopenic causes for hypopigmentation

Chemicals: Catechols

MBH

Phenols

Sulphydrils

Genetic: Ataxia telangiectasia

Piebaldism

Vitiligo

Waardenburg syndrome

Woolfe syndrome

Xeroderma pigmentosum

Inflammatory: Mycosis fungoides

Pityriasis lichenoides

chronica

Yaws,pinta

Neoplastic: Halo nevi

Physical: Burns, trauma

Miscellaneous: Scleroderma

### Melanopenic causes for hypopigmentation

Chemicals: Arsenic

Chloroquine

Glucocorticoids

Hydroquinone

Retinoids

Endocrine: Hypopituitarism

Hypothyroidism

Genetic: Hypomelanosis of ito

Nevus depigmentosus

Tuberous sclerosis

Inflammatory: Leprosy

Post kala-azar

Syphilis

Tinea versicolor

Sarcoidosis

Pityriasis alba

Postinflammatory

DLE, Seborrheic dermatitis

Eczemas, Psoriasis, Pityriasis lichenoides

Lichen striatus, PR, PLE<sup>40</sup>

Mycosis fungoides

Atopic dermatitis

Neoplastic: Melanoma

Nutrition: Protein loss

Kwashiorkor

Malabsorption

Physical: Post dermabrasion

Post laser

Miscellaneous: Idiopathic guttate

hypomelanosis

Non melanotic causes for hypopigmentation

Nevus anemicus

Woronoff's ring



## **Tinea Versicolor**

Syn: pityriasis versicolor, dermatomycosis furfuracea, tinea flavea, liver spots, chromophytosis

Tinea versicolor is a common superficial cutaneous fungal infection usually characterized by hypopigmented or hyperpigmented macules and patches on the chest and the back. In patients with a predisposition, the condition may chronically recur. The fungal infection is localized to the stratum corneum

### **Etiology**

The lipophilic fungus *Malassezia* is implicated as the causative organism. Various species involved are *M.furfur*, *M.symphodialis*, *M.globosa*, *M. restricta*, *M.obtusa*, *M. slooffiae* <sup>41,42</sup> and recently described *M.dermatis* <sup>43</sup>

In patients with clinical disease, the organism is found in both the yeast (spore) stage and the filamentous (hyphal) form.<sup>44</sup>

Predisposing factors that lead to the conversion of the saprophytic yeast to the parasitic, mycelial morphologic form include a genetic predisposition <sup>45</sup>; warm, humid environments<sup>46</sup>; immunosuppression<sup>47</sup>; malnutrition<sup>48</sup>; pregnancy ; Oral Contraceptive pills <sup>49</sup> and Cushing

disease<sup>50</sup>. Human peptide cathelicidin LL-37 plays a role in skin defense against this organism.<sup>51</sup>

## Pathogenesis

### Causes of hypopigmentation

1. Dicarboxylic acid produced by fungus inhibits tyrosinase<sup>52</sup>
2. Direct cytotoxicity of dicarboxylic acid<sup>52</sup>
3. Increased cell turnover of affected skin<sup>53</sup>
4. Filtering of UV rays by fungus and pityriacitrin, an indole compound produced by it leading to decreased tanning<sup>54</sup>
5. Decreased melanosomes in stratum spinosum<sup>55</sup>

The organism is lipophilic, and lipids are essential for growth in vitro and in vivo. Because the organism more rapidly colonizes humans during puberty when skin lipids are increased more than that of adolescent levels and tinea versicolor is manifested in sebum-rich areas (e.g., chest, back), individual variations in skin surface lipids are hypothesized to play a major role in disease pathogenesis.<sup>56</sup>

Another significant causative factor is the patient's immune system. Although sensitization against *M furfur* antigens is routinely present in the general population, lymphocyte function on stimulation with the

organism has been shown to be impaired in patients who are affected. In short, cell-mediated immunity plays some role in disease causation.<sup>57</sup>

### Clinical features

Although the alteration in skin pigmentation is more apparent in darker-skinned individuals, the incidence of tinea versicolor appears to be the same in all races. No dominance of either sex is apparent but there is difference in susceptibility in different ages.<sup>58</sup> In temperate climates the disease is most common in persons aged 15-24 years, when the sebaceous glands are more active. Its occurrence before puberty or after age 65 years is uncommon.<sup>53,59</sup> In more tropical countries, age frequency varies; most cases involve people aged 10-19 years who live in warmer, humid countries, such as Liberia and India.<sup>60</sup>

Tinea versicolor can present in 3 forms.<sup>61</sup>

The most common appearance of the disease is as numerous, well-marginated, finely scaly, oval-to-round macules scattered over the trunk and/or the chest, with occasional extension to the lower part of the abdomen, the neck, and the proximal extremities. The macules tend to coalesce, forming irregularly shaped patches of pigmentary alteration. As the name versicolor implies, the disease characteristically reveals a

variance in skin hue. The involved areas can be either hypopigmented or hyperpigmented.

An inverse form<sup>62</sup> of tinea versicolor also exists in which the condition has an entirely different distribution, affecting the flexural regions, the face, or isolated areas of the extremities. This form of tinea versicolor is more often seen in hosts who are immunocompromised.

The third form of M furfur infections of the skin involves the hair follicle. This condition is typically localized to the back, the chest, and the extremities as perifollicular, erythematous papules or pustules.

### Symptoms<sup>53</sup>

Most individuals with tinea versicolor complain of cosmetically disturbing, abnormal pigmentation. Occasionally, a patient also complains of mild pruritus.

### Diagnosis

The clinical presentation of tinea versicolor is distinctive, and the diagnosis is often made without any laboratory documentation.

The ultraviolet black (Wood) light can be used to demonstrate the golden yellow fluorescence of tinea versicolor<sup>61</sup>. The diagnosis is usually confirmed by potassium hydroxide (KOH) examination, which demonstrates the characteristic short, hyphae that are present in the diseased state. The KOH finding of spores with short mycelium has been referred to as the spaghetti and meatballs<sup>61</sup> sign of tinea versicolor. For better visualization, ink blue stain, Parker ink or methylene blue stain can be added.<sup>63</sup>

On histopathology the organism that causes tinea versicolor is localized to the stratum corneum. *M. furfur* can be detected by hematoxylin and eosin (H&E) alone, although periodic acid-Schiff (PAS) or methenamine silver staining are more confirmatory. On rare occurrences, the organism can approach the stratum granulosum, and it can even be found inside keratinocytes. The epidermis reveals mild hyperkeratosis and spongiosis, and a mild perivascular infiltrate is present in the dermis.

64-65

## **Vitiligo**

Vitiligo is a specific, common often acquired disorder characterized by well circumscribed milky white macules devoid of identifiable melanocytes.<sup>66</sup> Occasionally, the loss of melanin (i.e., hypopigmentation)

is partial. It is an acquired progressive disorder in which some or all of the melanocytes in the interfollicular epidermis, and occasionally those in the hair follicles, are selectively destroyed.<sup>67</sup>

### Epidemiology

Vitiligo is relatively frequent, with a rate of 1-2%. About 30% of cases occur with a familial clustering of cases<sup>68</sup>. There is female preponderance in most series but frequency in the population is probably the same in both sexes.<sup>69</sup>

Vitiligo may appear at any time from birth to senescence, though the onset is most commonly observed in persons aged 10-30 years. It rarely is seen in infancy or old age. Nearly all cases of vitiligo are acquired relatively early in life. The average age of onset is around 20 years.<sup>70</sup>

### History:

In early vitiligo, white areas are not distinct and may be pruritic. Hypomelanotic macules are first noted on sun exposed areas. Vitiligo primarily progresses without any symptoms. In late vitiligo, the tendency of the disease to spread can stop<sup>2</sup>. Precipitating factors in form of physical or mental stress or injury may be present<sup>39</sup>

### Clinical features<sup>39</sup>

Vitiligo appears as sharply circumscribed, cosmetically disturbing, milk white to chalky white macules and patches with scalloped margins measuring few to several centimeters. At first, only a few, small, and sharply circumscribed foci are present. The borders of these foci are often hyperpigmented. Lesions increase in number and become confluent. Trichrome, quadrichrome, pentachrome and inflammatory varieties have been described with varied pigmentary alterations.

### Clinical classification of vitiligo<sup>39</sup>

Vitiligo lesions may be localized or generalized, with the latter being more common than the former.

#### Localized

Focal - One or more scattered macules limited in size and number by vague convention. 20% of children have the focal pattern

Segmental - One or more macules in a unilateral dermatomal or quasidermatomal distribution. Trigeminal area being the commonest site

## Generalized

This is the most common type characterised by few to many widespread symmetrically placed macules usually over extensor surfaces.

Many of the most common sites of occurrence are areas subjected to repeated trauma, including the following: bony prominences, extensor forearm, ventral wrists, dorsal hands, digital phalanges, elbows and knees. Involvement of the mucus membrane is frequently observed in the setting of generalized vitiligo. Leukotrichia , canities, halo nevi and alopecia areata are associated.

Acrofacial vitiligo involves distal digits and periorificial areas while lip-tip vitiligo involves lips distal penis and nipples

Universal vitiligo implies complete or nearly complete depigmentation usually associated with multiple endocrinopathy syndrome.

Vitiligo may be associated with other autoimmune diseases, especially thyroid disease and diabetes mellitus. Other associated autoimmune diseases include pernicious anemia, Addison disease, myasthenia gravis and alopecia areata.<sup>2</sup>



Causes: Three pathogenic theories have been discussed <sup>71</sup>, as follows:

Immune hypothesis: Aberration of immune surveillance results in melanocyte dysfunction or destruction.

Neural hypothesis <sup>72</sup> : A neurochemical mediator destroys melanocytes or inhibits melanin production.

Self-destruction hypothesis: An intermediate or metabolic product of melanin synthesis causes melanocyte destruction.

A genetic hypothesis <sup>73</sup> postulating that melanocytes have an inherent abnormality of the endoplasmic reticulum that impedes their growth and differentiation has also been proposed.

## Diagnosis

Although the diagnosis of vitiligo generally is made clinically, biopsy is occasionally helpful in differentiating vitiligo from other hypopigmentary disorders. Early vitiligo few melanocytes in basal layer with superficial perivascular infiltrate as against complete loss of melanocytes in established cases of vitiligo. <sup>74,75</sup>

Thyroid-stimulating hormone (TSH) test is the most cost-effective screening test for thyroid disease. Screening for diabetes can be accomplished with a fasting blood sugar or glycosylated hemoglobin

### **Leprosy (Hansen's disease)**

Leprosy is a chronic granulomatous disease principally affecting the skin and peripheral nervous system, caused by *Mycobacterium leprae*. The earliest description of leprosy comes from India around 600 BCE. Armauer Hansen discovered M leprae in Norway in 1873. It was the first bacillus to be associated with human disease.<sup>76,77</sup>

The principal means of transmission is by aerosol spread from infected nasal secretions to exposed nasal and oral mucosa. Leprosy is not generally spread by means of direct contact through intact skin, though close contacts are most vulnerable<sup>78,79</sup>. The incubation period is 6 months to 40 years or longer. The mean incubation period is 2-5 years for tuberculoid leprosy (TT) and 8-12 years for lepromatous leprosy (LL)<sup>80</sup>. Approximately 77% of reported cases are found in 8 countries: Brazil, Democratic Republic of the Congo, India, Indonesia, Madagascar, Mozambique, Nepal, and the United Republic of Tanzania. Overall, the prevalence of the disease has decreased since the introduction of short-

course MDT in 1982. The global annual detection rate has also been declining since 2001<sup>81</sup>

Leprosy occurs in all races. It is more common in men than in women after puberty, with a male-to-female ratio of 2:1. Leprosy has a bimodal age distribution, with peaks at ages 10-14 years and 30-60 years. The disease is rare in infants. Children appear to be most susceptible to disease and tend to have the tuberculoid form.<sup>82</sup>

#### Clinical features<sup>83</sup>

Indeterminate leprosy: An early form causing one to a few hypopigmented or sometimes erythematous macules. Sensory loss is unusual. About 75% of affected persons have lesions that heal spontaneously. In some, the disease may persist in this indeterminate form. In those with weak immunity, the disease progresses to one of the other forms.

Tuberculoid leprosy: Skin lesions are single or very few. They may be macules or plaques which appear hypopigmented in dark skins and erythematous or copper coloured in light skins. They have a well-defined edge that is elevated indicating central healing or peripheral spread. They can be found on the face, limbs, or elsewhere, but are less common over intertriginous areas and the scalp. Lesions are hypesthetic

or definitely anaesthetic and are usually dry and scaly, hypohidrotic, and hairless. Neural involvement is common in TT and a thickened nerve is usually felt in the area around the skin lesion.

Borderline tuberculoid leprosy (BT): Lesions in this form are similar to those in the tuberculoid form but the marginal definition tends to be less pronounced with the margin being well defined in part of the lesion and vague in another. Lesions are more in number as against TT leprosy and also tend to be larger and associated with satellite lesions. Hypopigmentation, dryness and scaling tend to be less pronounced than true TT. Damage to peripheral nerves is more widespread and severe. Several large peripheral nerves are irregularly enlarged in asymmetric pattern. Type I reactions and deformities due to nerve damage are common.

Borderline lepromatous leprosy (BL): Lesions are numerous and consist of hypopigmented macules, papules, plaques, and nodules with a distribution tending toward symmetry. Nerve involvement may be widespread and signs of damage start sooner than LL. Cases downgraded from BT may show larger lesions and severe nerve involvement. Both Type I and Type II reactions are common.

Lepromatous leprosy (LL): Early cutaneous lesions consist mainly of hypopigmented macules. Macular lesions are small, diffuse, and

symmetric with smooth and shiny surface. Nerve involvement does not occur in LL until late, therefore early LL lesions have little or no loss of sensation, nerves are not thickened, and sweating is normal. Late lesions show infiltration and a waxy appearance. Nerve loss occurs slowly and progressively. Mucosal involvement and involvement of structures like eyes, bones, kidneys and liver is common.

### Diagnosis

Tissue smear testing/slit-skin smears are done for determining the Bacterial index (BI) as an indicator for bacterial load or Morphological index (MI) for disease activity and response to treatment.

### Histopathology<sup>84</sup>

In the Indeterminate form, findings are nonspecific. Histiocytes and lymphocytes are scattered, with some concentration around dermal appendages and nerves. No granulomas are seen. At times one or more acid-fast bacilli can be observed in a nerve bundle or arrector pili muscle.

In the TT form, well-developed epithelioid granulomas with giant cells are observed in the papillary dermis, often around neurovascular structures. The granulomas are surrounded by lymphocytes and hug the

epidermis with no Grenz zone. Dermal nerves are destroyed or swollen because of the granulomas. Acid-fast bacilli are rarely observed.

In the BT form, epidermis may show atrophy. Poorly organised epithelioid cell granulomas with few scattered Langhans giant cells and lymphocytes are seen in dermis. Few bacilli may be seen in dermal nerves as well as in the arrector pili. Nerves destruction due to granulomas is common. A subepidermal Grenz zone starts to form.

In the BL form, smaller granulomas with some foamy macrophages and numerous lymphocytes are observed. A clear grenz zone is seen. Nerves often have an onionskin appearance due to invasion of the epineuria. A few epithelioid cells may be observed. Numerous bacilli are seen in macrophages, schwann cells and adnexal structures.

In the LL form, epidermis is always atrophied. A diffuse infiltrate of foamy macrophages is present in the dermis below a subepidermal grenz zone. An enormous number of acid-fast bacilli are seen within the foamy macrophages, singly or in clumps called globi and also in schwann cells and adnexa. Lymphocytes are scant, and giant cells are typically absent. Focal collections of plasma cells may be seen.

## **Tuberous sclerosis**

Tuberous sclerosis is a genetic disorder affecting cellular differentiation and proliferation, which results in hamartoma formation in many organs (e.g., skin, brain, eye, kidney, heart). Sherlock coined the term epiloia, encompassing the clinical triad of epilepsy, low intelligence, and adenoma sebaceum.<sup>85</sup>

The inheritance is autosomal dominant, while up to 50-70% of cases have been attributed to new mutations. Two genetic loci have been identified so far. The first gene maps to chromosome 9, specifically 9q34 (TSC1); the second gene maps to chromosome 16, specifically 16p13 (TSC2)<sup>86,87</sup>.

Hypopigmented macules are found in 79 to 98 % of tuberous sclerosis patients. Four types of hypopigmented macules are recognised : lance ovate (ash leaf macules), polygonal macules, confetti spots and hypomelanosis in dermatomal distribution. Long axis of ash leaf macules is usually axial on the extremities and transverse on the trunk. Confetti macules (2-3 mm) occur from wrists to elbows and ankles to knee. Margins are fairly discrete and the colour is dull to off white. More than three hypomelanotic macules form one of the ten major criteria for diagnosis.<sup>39</sup>

Other features like facial angiofibromas, periungual fibromas, shagreen patch and history of epilepsy aid in diagnosis of the syndrome<sup>88</sup>

### **Piebaldism and Waardenburg syndrome**

Piebaldism is an uncommon, autosomal dominant, congenital, stable leukoderma characterised by a white forelock and amelanotic macules. The typical macule is chalk or milk white and may have feathered margins present over forehead, lateral trunk, midarm and legs, anterior abdomen and spares the midline, hands, feet and periorificial areas<sup>89</sup>. Lesions similar to Piebaldism occur in Waardenburg syndrome which also shows dystopia canthorum, congenital deafness and heterochromia irides.<sup>90</sup>

### **Hypomelanosis of Ito<sup>91,92</sup>**

This disorder also termed as pigmentary mosaicism of Ito is characterised by randomly distributed hypomelanotic macules with a bizarre whorled and streaked marble cake configuration. These lesions consist of bilateral and unilateral streaks corresponding to the lines of Blaschko.

Extracutaneous features are present in 75% patients. These include CNS, ophthalmological, dental defects and skeletal defects.



### **Nevus achromicus**<sup>93</sup>

Also known as nevus depigmentosus, this disorder presents at birth with stable hypomelanotic lesions in three forms: isolated circular or rectangular macule; dermatomal pattern; or a systematized (unilateral whorls or streaks form). Common sites are trunk and proximal extremities and it typically does not cross the midline.

### **Post Inflammatory hypomelanosis**

A number of inflammatory dermatosis may be associated with or may resolve to leave hypomelanotic macules corresponding to the cutaneous sites of involvement. This is commonly seen with eczematous dermatitis, psoriasis, pityriasis lichenoides chronica, pityriasis rosea, polymorphous light eruption, mycosis fungoides, discoid lupus erythematosus, lichen planus, lichen striatus and seborrheic dermatitis.<sup>40</sup>

Macules are tan to off white with indistinct margins and always correspond to the sites of prior eruption. This process is considered to be a result of a melanosome transfer block. Increased epidermal turnover may be responsible in psoriasis. Diagnosis rests on observation or history of associated dermatosis.<sup>39</sup>

Pityriasis rosea is an acute, self limiting skin eruption with a distinctive and constant course of a primary plaque ( Herald patch) followed after 1-2 weeks by a generalised secondary rash with a typical distribution and lasting for about 6 weeks. Sex incidence is almost equal and most patients are in age group 10 to 35 years. Various infections especially HHV-6 and HHV-7 have been implicated in etiology. Classical PR lesions are erythematous plaques with peripheral collarette of fine scaling over trunk and proximal extremities. Resolving stage frequently shows pigmentary disturbances in the form of hypo and hyperpigmentation. Histopathology is not pathognomic and shows patchy parakeratosis, decreased granular layer, acanthosis, spongiosis and superficial dermal infiltrate.<sup>94</sup>

Parapsoriasis is a group of disorders characterised by persistent, scaling inflammatory eruption. It includes three entities : large plaque parapsoriasis, small plaque parapsoriasis and pityriasis lichenoides<sup>95,96</sup>. Pityriasis lichenoides chronica occurs in early decades of life with a slight male predominance. It is characterised by successive crops of asymptomatic, red brown, oval to round, lichenoid papules with central adherent mica like scale over trunk and proximal extremities. A transient or more protracted leukoderma may result as the lesions evolve<sup>97</sup>. Histopathology shows acanthosis, hyperkeratosis with

characteristic lymphocytic exocytosis with dermal lymphocytic infiltrate in late lesions. CD 4+ subset of T cells predominate.<sup>97</sup>

Polymorphic light eruption is a common acquired disorder characterised clinically by the abnormal occurrence, within hours to a day or so of UVR exposure, of itchy, non scarring, erythematous papules, vesicles or plaques of some or all sun exposed skin. It usually has an onset in first three decades of life and affects females more commonly than males.<sup>98</sup> The lesions are generally symmetric and they resolve over days to week sometimes with post inflammatory hypopigmentation.<sup>40</sup> A delayed type hypersensitivity response to a sunlight-induced, cutaneous neoantigen first proposed in 1942 by Stephen Epstein has been proved to be the cause. Histopathology is not pathognomic .Early lesion show normal epidermis with dermal perivascular and periappendageal lymphohistiocytic infiltrate while late lesions show spongiosis and basal cell hydropic degeneration.<sup>99</sup>

Lichen striatus is an inflammatory papular eruption with a distinctive linear distribution often following Blaschko's lines<sup>100</sup>. It is self limiting and primarily occurs in children aged 5-15 years<sup>101</sup>. Post inflammatory hypopigmentation may be prominent in dark skinned persons <sup>40</sup>. Histopathological features suggest chronic lichenoid dermatitis with

parakeratosis, spongiosis, basal cell vacuolation, necrotic keratinocytes and superficial perivascular lymphohistiocytic infiltrate.<sup>102</sup>

Hypopigmentation in mycosis fungoides has been reported in darker skin types. Eruption clinically resembles tinea versicolor, generalised pityriasis alba, postinflammatory hypopigmentation or vitiligo. Involvement is more central than acral. Hypopigmentation is due to reduction in number of melanocytes and block in transfer of melanosomes to keratinocytes. Histologically it lacks epidermal atrophy and demonstrates moderate to marked exocytosis.<sup>39,40,103</sup>

Psoriasis is a common, chronic and inflammatory condition of the skin presenting with reddish scaly, sharply demarcated plaques commonly over extensor surfaces and scalp. Lesions usually resolve with postinflammatory hypopigmentation.<sup>39,40</sup> Histopathology is diagnostic with hyperkeratosis, parakeratosis, regular acanthosis, suprapapillary thinning of epidermis, Munro microabscesses, spongiform pustules of Kojog, dilation of dermal blood vessels and leukocytic dermal infiltrate.<sup>128</sup>

Pityriasis alba is a common hypomelanosis occurring predominantly in children over face but can occur over trunk and extremities.

Hypomelanosis is due to inflammation and UV screening effects of hyperkeratotic epidermis<sup>39</sup>

**Idiopathic guttate hypomelanosis (IGH)** <sup>39,104</sup>

IGH is a common acquired, discrete hypomelanosis affecting extremities of darker-skinned individuals. Typical lesions are very discrete, well circumscribed, porcelain white macules averaging 5mm in diameter. The lesions are few to many may increase in number and size with age and are most common in sun exposed areas of the extremities particularly anterior lower legs. A familial type has also been described

**Halo nevus** <sup>70,105</sup>

Also called Sutton's nevus it designates a halo of hypopigmentation around a central cutaneous tumour like benign melanocytic nevi, blue nevus, neurofibroma and primary or secondary malignant melanoma. The nevus is usually of the compound variety and tends to flatten and disappear. Autoimmune disorders are associated

**Nevus anemicus and Woronoff's ring** <sup>39</sup>: These are causes of hypopigmentation unrelated to melanin. Nevus anemicus is a congenital, localized vascular malformation presenting as off white macule which

becomes inapparent on diascopy. Woronoff's ring surrounds a psoriatic lesion and is also due to vascular changes

### **Miscellaneous causes**

Scleroderma may lead to amelanotic macules with perifollicular sparing resembling repigmenting vitiligo. Skin surrounding the hair follicles possesses a richer capillary network that may warm the perifollicular skin and preserve melanogenesis producing the perifollicular pigment retention in scleroderma <sup>106</sup>

Lichen sclerosus et atrophicus <sup>107</sup> also called white spot disease presents as symptom-less small ivory or porcelain white macules or papules commonly over the trunk and elsewhere. Genital lesions are very common and predispose to malignancy. Histopathological finding of band of hyalinised collagen below epidermis with sparse infiltrate is characteristic. Epidermis shows thickening, hyperkeratosis and follicular plugging but later becomes thinned out.

Epidermodysplasia verruciformis <sup>108</sup> is an inherited disorder in which widespread infection with HPV gives rise to combination of plane warts, pityriasis versicolor like lesions and reddish plaques. Plane warts on trunk present as scaly macular lesions which may be hypopigmented

closely resembling tinea versicolor. Histopathology reveals hyperkeratosis, acanthosis and extensive vacuolization of keratinocytes affecting upper half to three quarters of malphigian layer.

Infections like secondary syphilis, pinta, onchocerciasis, post kala azar dermal leishmaniasis can also cause hypopigmentation in late stages of infection .<sup>39</sup>

## **Aim**

1. To study the relative incidence of the various disorders causing a hypopigmented lesion in a random sample of 300 cases from the OPD cases at the Department of Dermatology, Madras Medical College, Chennai
2. To study the site, distribution and characteristics of the hypopigmented lesion in each of the diseases
3. To study the age and sex distribution of the commonest diseases presenting with a hypopigmented lesion
4. To make an attempt to classify the various conditions on basis of whether the hypopigmented lesion is scaly or non scaly
5. To look for the other conditions or systemic abnormalities associated with the diseases
6. To correlate the clinical findings with histopathology in selected cases



## **Materials and Methods**

A random sample of 300 patients presenting with one or more hypopigmented lesions to the out patient department of Department of Dermatology, Madras Medical College in the period October 2005 to April 2007 was studied. The inclusion and exclusion criteria were as follows

### **Inclusion Criteria:**

- The study included patients of pediatric as well as adult age group presenting with one or more hypopigmented lesions.
- Both scaly and non scaly presentations were included.

### **Exclusion Criteria:**

- Cases with depigmented lesions including those of established vitiligo, chemical leukoderma and leukoderma secondary to topical applications were excluded.
- Cases with lesions only over the face and/or mucosae and cases with generalised hypomelanosis were also excluded from the study.

Detailed history including address and occupation with special reference to onset and duration, preceding skin conditions, exposure to chemicals, topical application and family history was taken. Various characteristics of the lesion like site, size, number, distribution, surface and sensation were studied along with nail, hair, mucosal examination and examination of the palms and soles. Clinical photographs of all the cases were taken. Care was taken to find out any associated conditions coexisting with the primary disease. Relevant investigations including routine hemogram, VDRL, scraping for KOH smear, slit skin smear, Wood's lamp examination and skin biopsy were done. Analysis of each of the diseases was done and results compiled.

## Observations

The relative incidence of the various diseases presenting with a hypopigmented lesion in the 300 cases studied was as follows

S no.	Diagnosis	Incidence	Percentage
1	Tinea Versicolor	129	43 %
2	Postinflammatory hypopigmentation <ul style="list-style-type: none"> <li>- Polymorphous light eruption</li> <li>- Psoriasis</li> <li>- Pityriasis rosea</li> <li>- Parapsoriasis</li> <li>- Lichen striatus</li> <li>- Mycosis fungoides</li> <li>- Miscellaneous</li> </ul>	60 24 14 7 2 1 6	20% 8% 4.67% 2.33% 0.67% 0.33% 2%
3	Early Vitiligo	22	7.33%
4	Hansen's disease	19	6.33%
5	Nevus achromicus	4	1.33%
6	Tuberous sclerosis	2	0.67%
7	Scleroderma	2	0.67%

8	Lichen sclerosus et atrophicus	2	0.67%
9	Idiopathic guttate hypomelanosis	2	0.67%
10	Hypomelanosis of Ito	1	0.33%
11	Epidermodysplasia verruciformis	1	0.33%
12	Halo nevus	1	0.33%
13	Woronoff's ring	1	0.33%
	Total	300	100%

Among the 300 cases tinea versicolor was the most common diagnosis followed by post inflammatory hypopigmentation and early vitiligo. Polymorphous light eruption formed the major group causing post inflammatory hypopigmentation

### **Tinea Versicolor**

129 cases out of 300 presented with tinea versicolor with a male: female of 2.2: 1.

#### **Age and sex distribution in patients with Tinea Versicolor**

Age (years)	Male	Female
1-10	-	-
11-20	20	12
21-30	38	11
31-40	15	10
41-50	11	4
51-60	4	3
> 60	1	-
Total	89	40

Most common age group of presentation was 21-30 (49 cases). The most common site was upper trunk including chest and upper back. Neck, proximal arms and axillae were the other common sites noted. Abdomen, lower back and lower limbs were rarely involved.

### **Predominant site of involvement in cases with Tinea Versicolor**

Predominant site	Male	Female
Upper trunk	57	26
Upper arms and axillae	16	9
Neck	9	4
Abdomen, lower back, groin and lower limbs	5	1
Total	89	40

The lesions were hypopigmented, well defined patches with pencil line border, intact sensation and fine branny scaling which could be accentuated by grattage. Presentation varied from 1-5 discrete patches to greater than 10 patches coalescing at places to cover extensive areas. Scraping of the lesions followed by KOH mount showed blastospores surrounded by short straight or angulated hyphal fragments (spaghetti and meatball appearance) in 121 cases. Scraping for fungus was negative in 8 cases. 10 patients had associated seborrheic dermatitis, 12 had dermatophyte infection, 9 cases had acne and one case having associated Becker's nevus was seen

### Diseases associated with Tinea Versicolor

Associated disease	Number of patients
Dermatophyte infection	12
Seborrheic dermatitis	10
Acne	9
Becker's nevus	1

### Hansen's disease

19 cases were diagnosed as Hansen's disease based on clinical and histopathological findings. Male: Female ratio was 3.75:1 with maximum 9 cases presenting in the age group 20-30.

### Age and sex distribution in patients with Hansen's disease

Age (years)	Male	Female
0-10	1	-
11-20	3	1
21-30	6	3
31-40	3	-
41-50	2	-
>50	-	-
Total	15	4

All patients had more than one hypopigmented patch or plaque and two patients had more than 20 patches. In 17 cases lesions were hypopigmented non scaly plaques with borders well defined in some areas and ill defined in other areas. They had definite impairment of sensation with associated asymmetrical nerve thickenings. These cases were diagnosed as borderline tuberculoid leprosy. The two cases with more than 20 lesions had ill defined non scaly hypopigmented patches with subtle impairment of sensation. Lesions were distributed almost symmetrically and the cases were diagnosed as of borderline lepromatous leprosy.



### Subtype of Hansen's disease observed

Hansen Subtype	Number of patients	
	Male	Female
Borderline tuberculoid	13	4
Borderline lepromatous	2	-

One case of BL Hansen was in type II reaction. 5 cases of BT Hansen had associated deformities like trophic ulcer and claw hand. Biopsy from few cases of BT Hansen showed epithelioid cell granulomas. One case of BL Hansen showed diffuse macrophage granuloma with subepidermal grenz zone. Slit skin smear was positive in cases of BL leprosy with BI of 2+ .

### Early Vitiligo

22 patients were labeled as early vitiligo. Male: Female ratio was 1: 1.44 and the commonest age group of presentation being 20-30. Lesions were hypopigmented non scaly patches with ill defined margins and intact sensation. Lower limb was the commonest site

### **Age and sex distribution in patients with early vitiligo**

Age (years)	Male	Female
0-10	-	-
11-20	2	1
21-30	5	6
31-40	2	3
41-50	-	1
>50	-	-
Total	9	13

Associated mucosal lesions were present in 10 cases and leukotrichia in 9 cases. Family history of vitiligo was present in 6 cases. 3 patients had associated diabetes. On histopathology a normal epidermis apart from decreased to absent pigment in basal layer was seen.

### **Post inflammatory hypopigmentation**

90 cases were diagnosed as post inflammatory hypopigmentation with polymorphous light eruption being the commonest cause

### Polymorphous light eruption

60 out of 90 cases of postinflammatory hypopigmentation were diagnosed to be secondary to polymorphous light eruption. Male: female ratio was 1: 2.15 and commonest age group being 20-40 years.

#### Age and sex distribution in patients with PLE

Age (years)	Male	Female
0-10	-	-
11-20	1	3
21-30	4	10
31-40	7	16
41-50	4	8
51-60	3	2
>60	-	2
Total	19	41

The commonest site was dorsa of forearms (41 cases) followed by nape of neck.

### Site of involvement in cases of polymorphous light eruption

Site of involvement	Number of patients	
	Male	Female
Dorsum of forearms	12	32
Nape of neck and upper back	7	8
Chest	-	1

26 patients gave history of photosensitivity. Patients were usually involved in occupations requiring outdoor activities. Lesions were ill defined hypopigmented scaly patches and plaques with intact sensation. Few lesions showed central hyperpigmentation with a hypopigmented border. Histopathology from few patients showed acanthosis, spongiosis, basal cell degeneration with pigment incontinence and patchy periappendageal inflammatory infiltrate.

### Psoriasis

Psoriasis formed the next common group showing post inflammatory hypopigmentation with 24 cases. Male : Female ratio was 1.6:1 with no age predilection.

### Age and sex distribution of patients with Psoriasis

Age group	Male	Female
0-10	-	-
11-20	1	-
21-30	7	5
31-40	3	2
41-50	2	1
> 50	2	1
Total	15	9

23 patients were known cases of chronic stable plaque type psoriasis on treatment and one case was of guttate psoriasis. Extensor surfaces of limbs, chest, back and abdomen were the common sites involved.

Lesions were hypopigmented with scaling and other features of psoriasis like scalp scaling and nail changes were present. Auspitz sign was negative and diagnosis was confirmed by clinical and characteristic histopathological features.

### Pityriasis Rosea

14 cases were diagnosed as cases of resolving pityriasis rosea. Male:

Female ration was 1.4: 1 and commonest age group being 20-30 years.

#### **Age and sex distribution in patients with pityriasis rosea**

Age (years)	Male	Female
0-10	-	-
11-20	2	1
21-30	7	3
31-40	1	-
41-50	-	-
>50	-	-
Total	14	4

History in all patients was characteristic with appearance of a large round to oval scaly reddish skin lesion suggesting a herald patch followed by appearance of multiple smaller lesions all over the body with a short duration ranging from 4-6 weeks which resolved with the hypopigmentation. Examination showed multiple discrete hypopigmented scaly patches symmetrically distributed over trunk and proximal arms. Biopsy from the lesions revealed a chronic dermatitis picture. Serum VDRL was reactive in low dilutions in one patient.

### Parapsoriasis

7 patients were diagnosed as having hypopigmentation secondary to parapsoriasis of the pityriasis lichenoides chronica subtype.

#### **Age and sex distribution in patients with parapsoriasis**

Age (years)	Male	Female
0-10	-	-
11-20	1	1
21-30	1	1
31-40	2	-
41-50	-	1
>50	-	-
Total	4	3

Male: Female ratio was 1.3:1 and no specific age predominance was seen.

History of reddish scaly papular lesions over the body which resolved leaving the hypopigmentation was present. The hypopigmented lesions were ill defined macules and patches with mild branny scaling distributed over trunk and proximal extremities. One case showed the characteristic erythematous papules with adherent scales associated with

the hypopigmentation. Biopsies of lesions showed hyperkeratosis, parakeratosis, lymphocytic exocytosis and diffuse lymphocytic infiltrate localized to dermoepidermal junction and perivascular area.

### Lichen Striatus

2 male patients aged 10 and 12 years were diagnosed as having lichen striatus. Both had scaly hypopigmented macules coalescing to form patches associated with lichenoid papules distributed in a linear configuration unilaterally along the long axis of upper extremity. No nail changes were seen. Biopsy showed chronic dermatitis picture with acanthosis, spongiosis and dermal perivascular lymphohistiocytic infiltrate.

### Mycosis Fungoides

A 50 year old male patient presented with tumorous growths over the scalp and lower abdomen with associated multiple well defined arcuate hypopigmented scaly plaques over the abdomen and back. Biopsy showing lymphocyte exocytosis and T cell marker studies confirmed the diagnosis of Cutaneous T cell lymphoma.



### Miscellaneous

6 cases of post inflammatory hypopigmentation were seen secondary to varied causes. 2 cases were due to resolved bullous disorder. The other 4 cases showed hypopigmentation secondary to previous traumatic injury.

### **Naevus achromicus**

4 cases of nevus achromicus were seen. This included 2 adult males with isolated hypopigmented non scaly patches with irregular borders over the trunk present since birth and stable since then. One 6 year old boy with systematized type of nevus was seen with a large hypopigmented patch covering the left half of trunk with characteristic sharp cut off at midline. A one year old female baby with irregular patches over buttocks was also seen.

### **Tuberous sclerosis**

2 adult males with tuberous sclerosis were seen. Both had non scaly hypopigmented ash leaf macules with other associated manifestations like angiofibromas, periungual fibromas shagreen patch and history of epilepsy and mental retardation. One patient had hypopigmented confetti macules as well. Wood's lamp examination showed accentuation of the hypopigmented lesions.

**Scleroderma**

2 cases of scleroderma, a male aged 58 years and a female aged 40 years were seen showing hypopigmented patches with perifollicular sparing (salt pepper pigmentation). Associated indurated skin was present over face, trunk and extremities.

**Lichen sclerosus et atrophicus**

2 female patients aged 40 and 52 years with lesions of lichen sclerosus et atrophicus were seen. One of the patients had discrete porcelain white macules and papules coalescing to form plaques associated with atrophy over the lower limb. The other patient had a hypopigmented atrophic plaques over the buttocks. Biopsy showed thinned out epidermis with band of hyalinised collagen beneath the epidermis.

**Idiopathic guttate hypomelanosis**

2 patients in age group 50-60 presented with multiple discrete well defined hypopigmented macules over the lower limbs which were non scaly and asymptomatic with no increase in size since presentation. These were diagnosed as idiopathic guttate hypomelanosis.

**Hypomelanosis of Ito**

A 15 year old boy presented with unilateral hypopigmented macules arranged in a whorled and streaked pattern along the lines of Blaschko over the left lower abdomen and proximal lower limb. The patient did not have any associated CNS, ophthalmic and skeletal abnormalities. Diagnosis of Hypomelanosis of Ito was made

**Epidermodysplasia verruciformis**

A 4 year old boy presented with multiple hypopigmented well defined plaques all over the body resembling tinea versicolor. Biopsy showed hyperkeratosis, acanthosis with vacuolated keratinocytes involving upper three quarters of the stratum malphigii. A diagnosis of epidermodysplasia verruciformis was made.

One known case of psoriasis vulgaris with hypomelanotic ring surrounding the resolving lesions was seen and diagnosed as Woronhoff's ring. A case with a hypomelanotic patch surrounding a melanocytic nevus was seen (Sutton's nevus)

**Classifying the various diseases seen on the basis of nature of  
surface of the hypopigmented lesions (scaly/nonscaly)**

<u>Diseases with scaly lesions</u>	<u>Diseases with non scaly lesions</u>
Tinea versicolor Resolving pityriasis rose Pityriasis lichenoides chronica Resolving psoriasis Polymorphous light eruption Lichen striatus Epidermodysplasia verruciformis	Hansen's disease Early Vitiligo Hypomelanosis of Ito Nevus achromicus Idiopathic guttate hypomelanosis Tuberous sclerosis

## **Discussion**

In this study of 300 cases with hypopigmented lesions tinea versicolor and post inflammatory hypopigmentation were the commonest causes.

### **Tinea Versicolor**

This condition formed the majority of cases (129). The male predominance and commonest age group (21-30 years) seen in this study correlates with previous studies.<sup>109,110</sup> The commonest distribution was over upper chest, back and neck and lesions were hypopigmented, well defined with pencil line border and branny scaling as documented in literature.<sup>53,56,109,111</sup> Association with seborrheic dermatitis and Becker's nevus was seen and has been documented<sup>109,112</sup>. In this study association with acne and dermatophyte infection was also seen. Positive scraping for the fungus with spaghetti and meatball appearance on KOH mount was found in 121 cases out of 129 (94%). A previous study had reported 98% positivity.<sup>111</sup>

### **Early vitiligo**

22 cases of early vitiligo showed slight female preponderance consistent with previous reports<sup>69,113</sup>. The commonest site of lower extremities and age group 20-30 years also coincides with recent studies<sup>113-15</sup>. Associated diabetes seen in this study has been documented<sup>113,116</sup>. Lesions were ill defined, non scaly with associated mucosal involvement

and leukotrichosis in few cases. Biopsy findings were consistent with literature<sup>74,75</sup> and showed partial to complete loss of melanocytes in basal layer with mild dermal lymphocytic infiltrate.

### **Hansen's disease**

19 cases of Hansen's disease were seen and the male predominance was consistent with previous studies<sup>117</sup>. The predominance in age group 20-30 was against the reported bimodal distribution.<sup>82</sup> The commonest type seen was borderline tuberculoid which was also reported by Indian studies<sup>117,118</sup>. Lesions of BT Hansen were upto 20 in number, non scaly, well defined at some and ill defined at other areas with definite impairment of sensation associated with asymmetrical nerve thickening as cited in literature.<sup>83</sup> Associated deformities like trophic ulcer and claw hand were seen. In BL cases lesion were ill defined, non scaly with subtle loss of sensation and were almost symmetrical in distribution. Asymmetric nerve thickenings were seen and these findings correlate with literature.<sup>83</sup> None of the cases had positive slit skin smear. Skin biopsy findings were consistent with literature.<sup>84</sup>

### **Post inflammatory hypopigmentation**

Post inflammatory hypopigmentation formed the second major group in this study. Hypopigmentation following the commonest causes seen in this study i.e. polymorphous light eruption, psoriasis, pityriasis rosea and pityriasis lichenoides chronica has been documented.<sup>40</sup>

Polymorphous light eruption was the commonest cause and the predominance of young females (20-30 age group) seen in this study as well as the commonest sites of dorsa of forearms and nape of neck correlates with the description in literature<sup>98</sup>. Lesions were well defined and scaly sometimes with central hyperpigmentation. The histopathological findings were consistent with literature<sup>99</sup>.

Psoriasis was the next common cause of postinflammatory hypopigmentation. Lesions were well defined, scaly but auspitz sign was negative signifying resolution of the disease. The sites of involvement were consistent with literature but no age predilection was seen probably due to small sample size. The histopathology was diagnostic as cited in literature.<sup>128</sup>

Pityriasis rosea commonly resolves with hypopigmentation as seen in this study. The male predominance seen in this study does not confirm with earlier studies<sup>119,120</sup> but this could be coincidental. The common age group (10-30 years) though was consistent with the earlier

studies<sup>121</sup>. The lesions were well defined, scaly and distributed mainly over trunk and proximal extremities and this correlates with literature<sup>94</sup>. Biopsy findings correlated with literature but were not diagnostic. One patient had VDRL reactive in low dilutions this caused confusion with secondary syphilis but TPHA was negative in this patient.

Parapsoriasis of the pityriasis lichenoides type commonly causes hypopigmentation as seen in an Indian study.<sup>122</sup> Male sex predominance and the age distribution were similar to that seen in the earlier study<sup>122</sup>. No cases of PLEVA were seen in this study as against the earlier study. Biopsy of the lesions showed lymphocytic exocytosis and dermal perivascular infiltrate characteristic of PLC. No biopsy showed a lymphomatoid variant<sup>123</sup> described in literature.

#### Lichen striatus

Both the cases of lichen striatus had linear hypopigmented scaly lesions with lichenoid papules over upper extremities as in literature<sup>100</sup>. Nails were not involved. Biopsy was consistent with literature.<sup>102</sup>



### **Mycosis fungoides**

Hypopigmented lesions in mycosis fungoides have been reported frequently in literature.<sup>103,124,125</sup> The case seen in this study had tumorous growths over abdomen and scalp with well defined arciform hypopigmented lesions over trunk. Biopsy and T cell marker studies were diagnostic.

### **Nevus achromicus**

Both localized and systematized types of nevus achromicus were seen. Lesions were hypopigmented, non scaly, well defined stable since birth and were asymptomatic as described in literature<sup>39,91,92</sup>. A study of 20 cases of nevus achromicus<sup>126</sup> showed similar clinical presentation but extracutaneous features like mental retardation and seizures reported in the study were not seen in this study.

### **Tuberous sclerosis**

2 cases of tuberous sclerosis were seen with characteristic ash leaf macules which were well defined off white to milk white non scaly patches consistent with literature.<sup>39</sup> Both cases had history of seizures and mental retardation and other cutaneous features like adenoma sebaceum, periungual fibromas and shagreen patch essential for making

diagnosis.<sup>88</sup> One case had hypopigmented confetti macules over chest which is an uncommon site for such lesions.

### **Scleroderma**

2 cases of scleroderma with hypomelanotic patches with perifollicular sparing associated with atrophy as described in literature<sup>106</sup> were seen

### **Lichen sclerosus et atrophicus**

Hypopigmented atrophic lesions of extragenital lichen sclerosus et atrophicus were seen and diagnosis confirmed by biopsy. The findings of atrophic epidermis with glassy dermal collagen were consistent with literature.<sup>107</sup>

### **Idiopathic guttate hypomelanosis**

This is a common disorder in elderly and two such cases were seen with non scaly stable hypopigmented macules over lower limbs. The low incidence seen in this study could be due to the fact that the asymptomatic nature and occurrence over cosmetically unimportant sites of this condition prompts patients to ignore it and not seek treatment.

### **Hypomelanosis of Ito**

A case with characteristic whorled hypopigmented lesions along lines of Blascho was seen. No associated extracutaneous manifestations were seen in this case. Though according to literature 75% cases have extracutaneous manifestations, cases without any such abnormalities have been reported.<sup>127</sup>

### **Epidermodysplasia verruciformis**

Flat warts mimicking tinea versicolor have been described in literature<sup>108</sup> as manifestation of epidermodysplasia verruciformis. Case seen in this study had similar hypopigmented scaly lesions and diagnosis was made by histopathological finding of koilocytes throughout the thickness of epidermis. There was no evidence of cutaneous malignancy

Hypopigmentation around a melanocytic nevus has been frequently reported<sup>70,105</sup> and one such case was seen in this study as was a case of Woronoff's ring around psoriatic plaques.

Other disorders causing hypopigmented lesions like pityriasis alba, and piebaldism were not seen in this study because of exclusion of facial lesions which is the commonest site of occurrence for these diseases

## Conclusion

1. Tinea versicolor was the condition presenting most commonly with a hypopigmented lesion. Upper trunk was found to be the commonest site.
2. The other common diseases in descending order of frequency were postinflammatory hypopigmentation, early vitiligo and Hansen's disease.
3. Polymorphous light eruption was the most common cause of postinflammatory hypopigmentation followed by psoriasis, pityriasis rosea and parapsoriasis
4. Polymorphous light eruption was seen more commonly in females with dorsa of forearms and nape of neck being the commonest sites.
5. Male predominance was noted in almost all groups of diseases except polymorphous light eruption and early vitiligo.
6. 20-30 was the commonest age of presentation in almost all groups
7. Nevus achromicus formed the commonest cause among nevoid disorders.
8. Classification on basis of surface of hypopigmented lesions (scaly/non scaly)

### Scaly lesions

- Tinea versicolor
- Resolving pityriasis rosea
- Pityriasis lichenoides chronica
- Resolving psoriasis
- Polymorphous light eruption
- Lichen striatus
- Epidermodysplasia verruciformis

### Non scaly lesions

- Hansen's disease
- Early Vitiligo
- Hypomelanosis of Ito
- Nevus achromicus
- Idiopathic guttate hypomelanosis
- Tuberous sclerosis

9. Certain associations like seborrheic dermatitis, acne and dermatophytosis with tinea versicolor and diabetes with vitiligo were noted.
10. Histopathology was helpful in diagnosis of cases like psoriasis, parapsoriasis and Hansen's disease while it was not contributory in cases of pityriasis rosea.

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## Proforma

Name

Date:

Age/Sex

O.P/I.P No.

Occupation

Address

Chief complaints

History of present illness

- Onset

- Duration

- Progress

- H/o itching, burning over the lesion

- H/o any preceding skin lesion

- H/o any drug intake

- H/o any preceding physical trauma

- Thermal injury

- Mechanical injury or surgery

- Radiation injury e.g. UV rays



X rays, ionizing radiation

- H/o exposure to chemicals
- H/o genital lesion, sexual exposure history
- H/o constitutional symptoms
- H/o decreased or loss of sensation over  
the lesion
- H/o seizures or focal neurological  
defects
- H/s/o mental retardation
- H/o visual or hearing defects

Treatment history

History of past illnesses

- Diabetes mellitus, hypertension

Family history

- H/o consanguinity in parents
- H/o similar lesions in family

Personal history

- H/o delayed milestones in childhood

## General Examination

- Built and nutrition
- Orientation in time, place, person
- Pulse and BP
- Pallor
- Icterus
- Lymphadenopathy

## Systemic Examination

- Nervous system
- Cardiovascular system
- Respiratory system
- Per abdomen examination

## Dermatological examination

### Examination of the lesion

- Site
- Size
- Shape
- Colour
- Distribution
- Surface : Scaly/Non scaly
- Trophic changes
- Sensation

- Satellite lesions
- Thickened nerves around the lesion

Associated skin conditions

Scalp examination

Nail examination

Hair examination

Mucosal examination

## Investigations

- Routine hemogram
- LFT, RFT
- Random Blood Sugar
- Serum VDRL
- Scraping of lesion for KOH mount
- Wood's lamp examination
- Grattage
- Diascopy
- Slit skin smear
- Skin biopsy
- ENT, Dental reference